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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/607,631	06/27/2003	F. Chris Minion	08411-035001	5135

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EXAMINER	
BASKAR, PADMAVATHI	
ART UNIT	**PAPER NUMBER**
1645	

MAIL DATE	DELIVERY MODE
06/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/607,631	MINION ET AL.	
	Examiner	Art Unit	
	Padmavathi v. Baskar	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *6-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/23/07 has been entered.

Status of Claims

2. Claims 28-29 are canceled.

Claims 1-5 and 27 are under examination.

Claims 6-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention.

Claim Rejections - 35 USC 112, first paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4 Claims 1-5 and 27 are rejected under 35 U.5.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a purified immunogenic polypeptide or mutant polypeptide, composition and a kit , the amino acid sequence of which comprises at least eight consecutive residues or at least 12 consecutive residues of a sequence SEQ ID NO: 8.

The state of the art with respect to immunogenic polypeptides Roitt et al (Immunology, 1993, Mosby, St. Louis, p 7.7-7.8) teach that it is possible to produce antibodies to almost any part of an antigen, this does not normally happen in an immune response. It is usually found that only a certain areas of the antigen are particularly antigenic, and that a majority of antibodies bind to these regions. These regions are often at exposed areas on the outside of the antigen, particularly where there are loops of polypeptide that lack a rigid tertiary structure (p.7.7-7.8). This is exemplified by the teaching of Holmes (Exp. Opin.Invest. Drugs, 2001, 10(3):511-519) who teaches that rabbits were immunized with synthetic peptides which in each case generated high anti-peptide specific immunoreactivities, however, none of the antibodies exhibited binding to the full length antigen. The author concludes that 'Presumably, expression of these epitopes in the context of the protein was important and affected the antibody binding ability (p. 513, col 1). Furthermore, this does not take into account the 3 dimensional folding of the native

molecule, nor its glycosylation or other post-translational modifications and other characteristics which are of significant importance in an antibody response. Peptides or synthetic antigens cannot effectively substitute for the natural tertiary and quarterary structure of a protein in a physiological situation

The state of the art with respect to mutant polypeptides teach that for proteins, for example, even a single amino acid change can destroy the function of the biomolecule. The effects of these changes are largely unpredictable as to which ones have a significant effect versus not. The art teaches that the significance of any particular amino acid sequences (i.e. fragment) cannot be predicted a priori for different aspects of biological activity and must be determined empirically on a case-by-case basis (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6). Bowie et al (Science, 1990, 257:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function and carry out the instructions of the genome and further teaches that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (col 1, p. 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (col 2, p. 1306).

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." Id. At 1567, 43 USPQ2d at 1405. The court also stated that a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. " Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. Thus, the instant specification may provide an adequate written description of a purified immunogenic polypeptide, mutant polypeptide comprising at least eight consecutive residues or at least 12 consecutive residues of a sequence SEQ ID NO: 8 (hereafter referred to variants of SEQ.ID.NO:8), per Lilly by structurally describing a representative number of immunogenic variants of SEQ.ID.NO:8 "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not describe immunogenic variants of SEQ.ID.NO:8 in a manner that satisfies either the Lilly or Enzo standards. The specification does not provide the complete structure of immunogenic variants of SEQ.ID.NO:8.nor does the specification provide any partial structure of immunogenic variants of SEQ.ID.NO:8.nor any physical or chemical characteristics of immunogenic variants of SEQ.ID.NO:8.nor any functional characteristics coupled with a known or disclosed correlation between structure and function. Although the specification discloses a single purified immunogenic polypeptide comprising the amino acid sequence, SEQ.ID.NO:8 , this does not provide a description of polypeptide variants of SEQ.ID.NO:8 that would satisfy the standard set out in Enzo because an isolated recombinant polypeptide comprising 8 or more consecutive amino acids read on widely varying genus variants as the amino acid sequence SEQ ID NO: 8 contains 1879 amino acids, said genus is so diverse with many different species that the specification has not shown the common elements/function that all the claimed species have.

The specification also fails to describe polypeptide variants of SEQ.ID.NO:8 by the test set out in Lilly. The specification describes only a single polypeptide set forth as SEQ.ID.NO:8. Therefore, it necessarily fails to describe a "representative number" of such species. In addition, the specification also does not describe "structural features common to the members of the genus, which features constitute a substantial portion of the genus."

Thus, the specification does not provide an adequate written description of immunogenic polypeptide variants of SEQ.ID.NO:8. Since the specification fails to adequately describe the claimed polypeptide variants of SEQ.ID.NO:8 , it also fails to adequately describe composition or kit comprising said of using polypeptide variants of SEQ.ID.NO:8.

Further , Patent No. 6747137 as shown below discloses an immunogenic polypeptide fragment having at least 8 amino acids , however said fragment is 100% identical in structure with the claimed variant but obtained from Candida which has no functional relationship with Mycoplasma . Thus there is no correlation between structure and function

; Sequence 14200, Application US/09248796A
; Patent No. 6747137
; GENERAL INFORMATION:
; APPLICANT: Keith Weinstock et al
; TITLE OF INVENTION: NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO CANDIDA ALBICANS
; TITLE OF INVENTION: FOR DIAGNOSTICS AND THERAPEUTICS
; FILE REFERENCE: 107196.132
; CURRENT APPLICATION NUMBER: US/09/248,796A
; CURRENT FILING DATE: 1999-02-12
; PRIOR APPLICATION NUMBER: US 60/074,725
; PRIOR FILING DATE: 1998-02-13
; PRIOR APPLICATION NUMBER: US 60/096,409
; PRIOR FILING DATE: 1998-08-13
; NUMBER OF SEQ ID NOS: 28208
; SEQ ID NO 14200
; LENGTH: 665
; TYPE: PRT
; ORGANISM: Candida albicans
US-09-248-796A-14200

Query Match 0.7%; Score 14; DB 4; Length 665;
Best Local Similarity 100.0%; Pred. No. 0.00061;
Matches 14; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy       1258 QQQQQQQQQQQQQP 1271
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Db        583 QQQQQQQQQQQQQP 596
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Claims 1-5 and 27 do not comply with 35 USC 112, first paragraph because it is not supported by an adequate written description in the specification.

Applicants argues that the claimed polypeptide are only directed toward those polypeptides that elicit an antibody response. Therefore, this language serves to limit the claims to only those polypeptides that exhibit this property. In addition, the specification discloses how to obtain and identify immunogenic polypeptides. See, for example, page 20, lines 22-31 of the specification. Further, the specification exemplifies a number of different immunogenic polypeptides of a variety of different lengths including 7, 9, 12 and 15 residues in length. See, for example, page 29, lines 1-7; page 31, lines 19-25; page 34, line 20-page 35, line 20; page 37, line 13 - page 38, line 5; page 40, lines 6-7; page 41, lines 15-17; and page 49, lines 3-5 of the specification. Therefore, Applicants were clearly in possession of the genus of immunogenic polypeptides at the time the application was filed.

Applicants argument is considered but found to be non-persuasive because some of applicant's arguments drawn to previous rejection of the claims under 35 USC 112, first paragraph are relevant to the instant rejection. Applicant is arguing the limitations such as specific length peptides and peptides elicit an antibody response etc are not set forth in the claims. Further , the claimed polypeptide is a 1879 amino acids sequence comprising many peptides including 7,9,12 and 15 etc that might induce an antibody response (function) . A definition by function, as previously indicated, does not suffice to define the genus because it is only an indication of what the peptide does, rather than what it is. Further , there are many peptides in the claimed polypeptide that induce an antibody, however, they can not be distinguished from each other because all of them elicit antibody.

Applicant states that five different immunogenic polypeptides are disclosed in the specification, SEQ.ID.NO:34, 36, 39, and 41 etc.

Applicants argument is considered but found to be non-persuasive because the claims are not drawn to specific length peptides SEQ.ID.NO:34, 36, 39, and 41 .

Applicant argues that the written description requirement must be applied in the context of the particular invention and the state of knowledge in the art and points to *Capon v. Eshhar* wherein it was found that "when the prior art includes the nucleotide information, precedent does not set a per se rule that the information must be determined afresh".

The arguments have been considered but have not been found persuasive because Applicant has not demonstrated a nexus between the fact pattern in the instant specification and that in *Capon v. Eshhar*. In particular, although Applicant points to the ruling wherein if the sequence information is known in the prior art, it is unnecessary to provide it a new, although the specification provides SEQ ID NO:8, the sequences of the claimed variants are not in fact known. Given the above, although Applicant suggests a similarity between the claims of the instant invention and the claims reviewed in the Eshhar case, Examiner fails to see any similarity between the two cases. In particular, unlike the known structure of the

Eshhar claims, the structure of the broadly claimed variants is unknown because no structure function relationship has been identified for either the raising of antibodies which recognize full-length SEQ ID NO:8, or the recognition by T-cells from M. hyopneumoniae infected samples . Similar to the Lilly case, the broadly claimed, unknown structures are critical to the instant invention. Thus, the citation, by Examiner of Lilly is appropriate. Further, the Court, in *Capon v. Eshhar*, stated that it is appropriate to recognize the variability in the science in determining the scope of coverage to which the inventor is entitled and that the decision as to whether the claimed scope is appropriate usually focuses on the exemplification in the specification and the Court pointed specifically to Lilly and stated that the genus is not described where "a representative number of cDNAs defined by nucleotide sequence, falling within in the scope of the genus" had not been provided. Similar to the Lilly case, a representative number of variants which can be used as immunogens to raise antibodies which recognize full-length SEQ.ID.NO:8 or are recognized by T-cells from M. hyopneumoniae infected samples, except SEQ ID NO:8, falling within the scope of the genus has not been provided. The arguments have been considered but have not been found persuasive and the rejection is maintained.

7. Claims 1-5 and 27 are rejected under 35 U.5.C. 112, first paragraph because the specification, while being enabling for an isolated and purified immunogenic polypeptide, composition and kit comprising the amino acid sequence SEQ.ID.NO:8, the specification does not reasonably provide enablement for an isolated polypeptide, a composition, and a kit comprising a purified polypeptide comprising 8 or 12 consecutive amino acid sequence of SEQ.ID.NO: 8 (The examiner is considering all these as variants). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims is maintained as set forth in the previous office action.

The instant claims are evaluated for enablement based on the Wands analysis. Many of the factors regarding undue experimentation have been summarized in *In re Wands*, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:

(1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The claims are drawn to a purified immunogenic polypeptide or mutant polypeptide, composition and a kit , the amino acid sequence of which comprises at least eight consecutive residues or at least 12 consecutive residues of a sequence SEQ ID NO: 8 (these polypeptide are considered and referred to variants of SEQ.ID.NO:8)

This means that the claimed polypeptide is broadly drawn to undefined immunogenic polypeptide comprising at least 8 or 12 consecutive amino acid of SEQ ID NO:8 that can be made and used for detecting antibodies to SEQ.ID.NO:8 and is not limited to SEQ ID NO:8.

The nature of the disclosed invention is preparing a recombinant polypeptide SEQ.ID.NO: 8 from *Mycoplasma hyopneumoniae* strain 232. The specification indicates that the claimed an isolated recombinant polypeptide comprising the amino acid sequence SEQ ID NO: 8 that contains 1879 amino acids. The instant inventors believe that the immunogenic or mutant polypeptides are likely responsible for the induction antibodies when immunized and said antibodies recognize or bind to the polypeptide comprising the amino acid sequence , SEQ.ID.NO:8.

One cannot extrapolate the teaching of the specification to the scope of the claims because the claims as written are drawn to variants of SEQ ID NO:8 with undefined alterations of the 1879 amino acid residues of SEQ ID NO:8 as well as undefined variants which comprise at least 8 or 12 consecutive residues of SEQ ID NO:8 and neither the specification nor the art of record define which amino acid residues are critical to the raising of antibodies that are specific for SEQ ID NO:8. As drawn to mutant polypeptides, Bowie et al (Science, 1990, 257:1306-1310), teaches that an amino acid sequence encodes a message that determines the shape of a protein and determines the ability of said protein to fold into unique three-dimensional structures that allows them to function. Bowie further teaches that certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (p. 1306, cols 1 and 2). As drawn to immunogenic polypeptide , clearly, the three dimension structure of a protein is critical to the production of antibodies given the teaching of Herbert et al (The Dictionary of Immunology, Academic Press, 3rd Edition, London, 1985, pages 58-59). Herbert et al who specifically teach that an epitope is the region on an antigen molecule to which antibody specifically binds. B cell epitopes on protein antigens are of variable size comprising up to about 20 amino acids. Antibodies bind in a more or less exact three dimensional fit with an epitope. This may be formed from residues on different regions of a protein antigen molecule which, in the native state, are closely apposed due to protein folding. Thus the three-dimensional structure of the protein molecule may be essential for antibody binding. (p. 58). However, neither the specification nor the art of record provide teachings that provide information about the residues critical for epitopes required for the establishment of an immune response that will produce antibodies that recognize full-length polypeptide, SEQ.ID.NO:6. This information appears to be critical because the art recognizes (see Bowie above) that it is the protein sequence that determines the three dimensional shape of a protein and Herbert et al specifically state that antibodies bind in a more or less exact three dimensional fit and suggests that the three-dimensional structure of the protein molecule may be essential for antibody binding. Thus, in the absence of guidance in the specification and one could not determine how to make the claimed invention or predict that any particular linear peptide would function as claimed with a reasonable expectation of success. Neither the art nor the specification as originally

filed provides guidance on how to determine which 15 or 20 amino acids will be capable of, when used as an immunogen, raising antibodies which bind specifically to SEQ ID NO:2. In particular, Roitt et al (Immunology, 1993, Mosby, St. Louis, p 7.7-7.8) teach that although it is possible to produce antibodies to almost any part of an antigen, this does not normally happen in an immune response. It is usually found that only a certain areas of the antigen are particularly antigenic, and that a majority of antibodies bind to these regions. These regions are often at exposed areas on the outside of the antigen, particularly where there are loops of polypeptide that lack a rigid tertiary structure (p.7.7-7.8). This is exemplified by the teaching of Holmes (Exp. Opin.Invest. Drugs, 2001, 10(3):511-519) who teaches that rabbits were immunized with synthetic peptides which in each case generated high anti-peptide specific immunoreactivities, however, none of the antibodies exhibited binding to the full length antigen. The author concludes that 'Presumably, expression of these epitopes in the context of the protein was important and affected the antibody binding ability' (p. 513, col 1). Furthermore, the specification does not take into account the 3 dimensional folding of the native molecule, nor its glycosylation or other post-translational modifications and other characteristics which are of significant importance in an antibody response. Peptides or synthetic antigens cannot effectively substitute for the natural tertiary and quarterary structure of a protein in a physiological situation. Given this teaching, even if the claimed peptides consists of 8 or 12 amino acid residues that were 100% identical to portions of SEQ ID NO:8 it would not be possible to determine with any predictability whether the antibodies produced from said peptide would be for SEQ ID NO:8 and actually bind to SEQ ID NO: 8 in the absence of guidance from the specification. However, the issues drawn to the lack of guidance in the specification as to critical residues and polypeptide fragments required for binding are relevant to this limitation as well. Further, there is no teaching in the specification of whether or not the epitopes are linear or comprise 3-dimensional structures. In particular, Greenspan et al (Nature Biotechnology, 1999, 7:936-937) teaches that defining epitopes is not as easy as it seems. Even when the epitope is defined, in terms of the spatial organization of residues making contact with ligand, then a structural characterization of the molecular interface for binding is necessary to define the boundaries of the epitope (page 937, 2nd column).

As drawn specifically to the polypeptides comprising the 8 or 12 amino acids of SEQ ID NO:2, Coleman et al. (Research in Immunology, 1994; 145(1): 33-36) teach that a single amino acid changes in an antigen can effectively abolish antibody antigen binding. Furthermore, Abaza et al. (Journal of Protein Chemistry, Vol. 11, No. 5, 1992, pages 433-444, see abstract in particular) teach single amino acid substitutions outside the antigenic site on a protein affects antibody binding. Clearly if antibody binding is abolished, it is because of the alteration of the conformation of the epitope to which the antibody binds. Given the clear teaching drawn to conformation alteration with even a single amino acid change, clearly it would be expected that amino acid residues outside of the antigenic epitope, not native to SEQ ID NO:8 would alter the conformation of that epitope in the polypeptide comprising and that it could not be predicted, nor would it be expected that a structurally altered antigenic epitope would

produce, for example, antibodies that would bind to SEQ ID NO:8. Further , Patent No. 6747137 as shown below discloses an immunogenic polypeptide fragment having at least 8 amino acids , however said fragment is 100% identical in structure with the claimed variant but obtained from Candida which has no functional relationship with Mycoplasma.

Sequence 14200, Application US/09248796A

; Patent No. 6747137
; GENERAL INFORMATION:
; APPLICANT: Keith Weinstock et al
; TITLE OF INVENTION: NUCLEIC ACID AND AMINO ACID SEQUENCES RELATING TO CANDIDA ALBICANS
; TITLE OF INVENTION: FOR DIAGNOSTICS AND THERAPEUTICS
; FILE REFERENCE: 107196.132
; CURRENT APPLICATION NUMBER: US/09/248,796A
; CURRENT FILING DATE: 1999-02-12
; PRIOR APPLICATION NUMBER: US 60/074,725
; PRIOR FILING DATE: 1998-02-13
; PRIOR APPLICATION NUMBER: US 60/096,409
; PRIOR FILING DATE: 1998-08-13
; NUMBER OF SEQ ID NOS: 28208
; SEQ ID NO 14200
; LENGTH: 665
; TYPE: PRT
; ORGANISM: Candida albicans
US-09-248-796A-14200

Query Match 0.7%; Score 14; DB 4; Length 665;
Best Local Similarity 100.0%; Pred. No. 0.00061;
Matches 14; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Qy       1258 QQQQQQQQQQQQQP 1271
              ||||||||||||||
Db        583 QQQQQQQQQQQQQP 596
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The specification provides no guidance or working examples which would provide guidance to one skilled in the art as to which amino acids of polypeptide are critical to the induction of an immune response specific for SEQ ID NO:8 and no evidence has been provided which would allow one of skill in the art to predict which of the broadly claimed polypeptide variants would function as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention.

Thus, it would not be expected that the claimed variants of SEQ.ID.NO:8 in the absence of further guidance from the specification, would function as claimed or as contemplated given that there is no teaching of residues critical to the claimed function. Further one would not know how to use of said variants that induce response and do not bind to the full length SEQ ID NO:8..

Applicant argues that based on the 'Wands factors' and consideration of the evidence as a whole, the pending claims are fully enabled by the present specification. Further, Hybritech Inc. v. Monoclonal Antibodies, Inc. cited in the previous response is relevant to the amount of experimentation that is considered to be undue. Hybritech Inc. v. Monoclonal Antibodies, Inc. stands for the proposition that even a large amount of experimentation is not undue if that experimentation is routine. Therefore, the pending claims are enabled.

Applicants argument is considered but found to be non-persuasive because some of applicant's arguments drawn to previous rejection of the claims under 35 USC 112, first paragraph are relevant to the instant rejection. Unlike in the Hybritech Inc. v. Monoclonal Antibodies, Inc , there is no teaching of residues critical to the claimed function in the claimed variants and therefore, the experimentation is undue as discussed above in the instant rejection.

Claim Rejections - 35 USC 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-5 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by database Uniprot_03, Accession number Q9KGX7 or. Q9KGX9

The Claims are drawn to a purified immunogenic polypeptide or mutant, the amino acid sequence of which comprises at least eight consecutive residues or at least 12 consecutive residues of a sequence SEQ ID NO: 8, Claims are also drawn to a composition and a kit comprising said polypeptide SEQ ID NO: 8.

Accession number Q9KGX7 disclose polypeptide comprising 8 or 12 consecutive residues of SEQ.ID.NO: 8 (see the sequence alignment of Q9KGX7 with the claimed SEQ.ID.NO:8).

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AC   Q9KGX7;
DT   01-OCT-2000 (TrEMBLrel. 15, Created)
DT   01-OCT-2000 (TrEMBLrel. 15, Last sequence update)
DT   01-OCT-2000 (TrEMBLrel. 15, Last annotation update)
DE   YX2 (Fragment).
GN   Name=yx2;
OS   Mycoplasma hyopneumoniae.
OC   Bacteria; Firmicutes; Mollicutes; Mycoplasmataceae; Mycoplasma.
OX   NCBI_TaxID=2099;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=J;
RA   Liao X., Papazisi L., Geary S.;
RL   Submitted (JUN-2000) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AF279293; AAF87783.1; -.
FT   NON_TER     560    560
SQ   SEQUENCE   560 AA;  63810 MW;  88AAC16175B7AE97 CRC64;
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 Query Match             11.0%;  Score 206;  DB 2;  Length 560;
  Best Local Similarity   100.0%;  Pred. No. 4.7e-196;
  Matches  206;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 MKNKKSTLLLATAAAIIGSTVFGTVVGLASKVKYRGVNPTQGVISQLGLIDSVAFKPSIA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MKNKKSTLLLATAAAIIGSTVFGTVVGLASKVKYRGVNPTQGVISQLGLIDSVAFKPSIA 60

Qy         61 NFTSDYQSVKKALLNGKTFDPKSSEFTDFVSKFDFLTNNGRTVLEIPKKYQVVISEFSPE 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 NFTSDYQSVKKALLNGKTFDPKSSEFTDFVSKFDFLTNNGRTVLEIPKKYQVVISEFSPE 120

Qy        121 DDKERFRLGFHLKEKLEDGNIAQSATKFIYLLPLDMPKAALGQYSYIVDKNFNNLIIHPL 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        121 DDKERFRLGFHLKEKLEDGNIAQSATKFIYLLPLDMPKAALGQYSYIVDKNFNNLIIHPL 180

Qy        181 SNFSAQSIKPLALTRSSDFIAKLNQF 206
              |||||||||||||||||||||||||||
Db        181 SNFSAQSIKPLALTRSSDFIAKLNQF 206
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Or

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ID   Q9KGX9      PRELIMINARY;      PRT;   560 AA.
AC   Q9KGX9;
DT   01-OCT-2000 (TrEMBLrel. 15, Created)
DT   01-OCT-2000 (TrEMBLrel. 15, Last sequence update)
DT   01-OCT-2000 (TrEMBLrel. 15, Last annotation update)
DE   YX2 (Fragment).
GN   Name=yx2;
OS   Mycoplasma hyopneumoniae.
OC   Bacteria; Firmicutes; Mollicutes; Mycoplasmataceae; Mycoplasma.
OX   NCBI_TaxID=2099;
RN   [1]
RP   SEQUENCE FROM N.A.
RC   STRAIN=ISU 232;
RA   Liao X., Papazisi L., Geary S.;
RL   Submitted (JUN-2000) to the EMBL/GenBank/DDBJ databases.
DR   EMBL; AF279292; AAF87781.1; -.
FT   NON_TER     560    560
SQ   SEQUENCE   560 AA;  63805 MW;  C1A89B69D7C04A18 CRC64;
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  Query Match             24.4%;  Score 459;  DB 2;  Length 560;
  Best Local Similarity   99.8%;  Pred. No. 0;
  Matches  559;  Conservative    0;  Mismatches    1;  Indels    0;  Gaps    0;

Qy          1 MKNKKSTLLLATAAAIIGSTVFGTVVGLASKVKYRGVNPTQGVISQLGLIDSVAFKPSIA 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db          1 MKNKKSTLLLATAAAIIGSTVFGTVVGLASKVKYRGVNPTQGVISQLGLIDSVAFKPSIA 60

Qy         61 NFTSDYQSVKKALLNGKTFDPKSSEFTDFVSKFDFLTNNGRTVLEIPKKYQVVISEFSPE 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db         61 NFTSDYQSVKKALLNGKTFDPKSSEFTDFVSKFDFLTNNGRTVLEIPKKYQVVISEFSPE 120

Qy        121 DDKERFRLGFHLKEKLEDGNIAQSATKFIYLLPLDMPKAALGQYSYIVDKNFNNLIIHPL 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Db        121 DDKERFRLGFHLKEKLEDGNIAQSATKFIYLLPLDMPKAALGQYSYIVDKNFNNLIIHPL 180

Qy        181 SNFSAQSIKPLALTRSSDFIAKLNQFNNQDELWVYLEKFFDLEALKANIRLQTADFSFEK 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        181 SNFSAQSIKPLALTRSSDFIAKLNQFNNQDELWVYLEKFFDLEALKANIRLQTADFSFEK 240

Qy        241 GNLVDPFVYSFIRNPQNQKEWASDLNQDQKTVRLYLRTEFSPQAKTILKDYKYKDETFLS 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        241 GNLVDPFVYSFIRNPQNQKEWASDLNQDQKTVRLYLRTEFSPQAKTILKDYKYKDETFLS 300

Qy        301 SIDLKASNGTSLFANENDLKDQLDVDLLDVSDYFGGQSETITSNSQVKPVPASERSLKDR 360
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        301 SIDLKASNGTSLFANENDLKDQLDVDLLDVSDYFGGQSETITSNSQVKPVPASERSLKDR 360

Qy        361 VKFKKDQQKPRIEKFSLYEYDALSFYSQLQELVSKPNSIKDLVNATLARNLRFSLGKYNF 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        361 VKFKKDQQKPRIEKFSLYEYDALSFYSQLQELVSKPNSIKDLVNATLARNLRFSLGKYNF 420

Qy        421 LFDDLASHLDYYFLVSKAKIKQSSITKKLFIELPIKISLKSSILGDQEPNIKTLFEKEVT 480
              |||||||||||  ||||||||||||||||||||||||||||||||||||||||||||||
Db        421 LFDDLASHLDYTFLVSKAKIKQSSITKKLFIELPIKISLKSSILGDQEPNIKTLFEKEVT 480

Qy        481 FKLDNFRDVEIEKAFGLLYPGVNEELEQARKAQRASFEKEKSKKGLKEFSQQKEENSKAI 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        481 FKLDNFRDVEIEKAFGLLYPGVNEELEQARKAQRASFEKEKSKKGLKEFSQQKEENSKAI 540

Qy        541 NNQEGLEEDDNITERLPENS 560
              ||||||||||||||||||||
Db        541 NNQEGLEEDDNITERLPENS 560
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The disclosed polypeptide comprises 560 amino acids that contains 8 or 12 consecutive residues of SEQ.ID.NO: 8 and is 100% identical with the claimed immunogenic polypeptide of claim 1 and 2. The same polypeptide Q9KGX7reads on claim 4 mutant as the prior art polypeptide contains amino acid Aspartic acid "D" in place of Glutamic acid "E at position 544. The art teaches that an immunogenic polypeptide (i.e., antigen or epitope) is roughly 5 amino acids in size and can elicit an immune response and react with an antibody. Therefore, the disclosed polypeptide meets the limitation of claims 1-2 and 4. The same polypeptide Q9KGX7 read on the composition claims 3 and 5 (composition contains only immunogenic polypeptide) because the disclosed polypeptide to which an immune response has to be elicited is in general in hydrophilic phase, buffer or saline and is routinely used in the art. Similarly immunogenic polypeptide Q9KGX7 reads on the kit claim 27 because the claimed kit contains only polypeptide, which binds to an antibody. Thus the prior art anticipated the claimed invention.

Applicants' Applicant argues that the cited reference does not disclose a 'purified' polypeptide.

Applicants argument is considered but found to be non-persuasive because there is no evidence provided by the applicant to show these polypeptides are not purified.

10. Claims 1-5 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang et al Infect. Immun., Mar 1995, 1013-1019, Vol 63, No. 3.

The transitional phrase or term "comprises" similar to the phrases or terms, such as, "has", "includes," "contains," or "characterized by," represents open-ended claim language and therefore does not exclude additional, unrecited elements. See M.P.E.P 2111.03 [R-1]. See *Molecular Research Corp. v. CBS, Inc., 793 F2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App.1948)* ("comprising" leaves "the claim open. for the inclusion of unspecified ingredients even in major amounts". On the other hand, the limitation "consisting of represents closed claim language and excludes any element, step, or ingredient not specified in the claim. In *re Gray, 53 F. 2d 520, II USPQ 255 (CCPA 1931); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948).*

Claims have been described supra.

Zhang et al 1995 disclose purified (Affinity chromatography) Mycoplasma proteins from pathogenic *M. hyopneumoniae* strains 232, 2A3 and 232 FA1 in PBS containing CHAPS (see page 1013, right column, first paragraph and 1014, left column, last paragraph). This composition contains purified immunogenic polypeptides SEQ.ID.NO: 8 and mutants of said polypeptide. The composition comprising purified polypeptides in PBS read on the claimed invention as it contains immunogenic polypeptides such as 97 kD that reacted predominantly with monoclonal antibody (see Fig. 1). The prior art composition read on the kit claim 27 because the claimed kit contains only polypeptide, which binds to monoclonal antibody and the disclosed polypeptide also binds to (MAb), F2G5. Thus the prior art anticipated the claimed invention.

Applicant's use of the open-ended term "comprising "in claims 1-5 and 27 fails to exclude unrecited steps or ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts. Therefore, the claims read on the disclosed composition comprising purified proteins such as 97 kD polypeptide. Thus the prior art anticipated the claimed invention. In the absence of evidence to the contrary the disclosed prior art proteins in PBS is the same as claimed polypeptide and composition. Since the Office does not have the facilities for examining and comparing applicants' product polypeptide with the product of the prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant argues that Zhang et al's product comprises purified P97 as well as other general population of adhesin polypeptides.

Applicants argument is considered but found to be non-persuasive because there is no evidence provided by the applicant to show what other adhesin polypeptides are present in the prior art polypeptide P97. Further, the use of the open-ended term "comprising "in claims 1-5 and 27 fails to exclude unrecited steps or ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts.

Remarks

11. No claims are allowed.

12. Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform to the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Right Fax number is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PMR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PMR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PMR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Padma Baskar Ph.D., whose telephone number is ((571) 272-0853. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 6.30 a.m. to 4.00 p.m. except First Friday of each bi-week.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600 .

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER

Padma Baskar Ph.D.